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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,189	09/30/2004	Paul Howley	22996	7534

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EXAMINER

HURT, SHARON L

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 06/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/510,189	Applicant(s) HOWLEY ET AL.	
	Examiner Sharon Hurt	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-27 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>September 30, 2004</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims refer to "a homology at least 50%", "a homology at least 60%" and "a homology of 65-75%". The standard for which the homology is compared against is not included in the claim. While the specification (at page 1) defines homologous genes in the present application as homologous to each other, rather than homologous to the poxvirus genome, it is not completely clear that the percent homology referenced in the present claims is as compared to each other. Insertion of the language "in comparison to each other" into the claims would be remedial.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 provides for the use of the recombinant poxvirus of claim 1, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is

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indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 19 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 26 recites the limitation "administering the DNA sequence to said cells" in lines 3 and 4. The claim drawn to "the DNA sequence" lacks antecedent basis in claim 1.

Claim 27 recites the limitation "administering the DNA sequence to said virus" in lines 3 and 4. The claim drawn to "the DNA sequence" lacks antecedent basis in claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring ingenuity beyond that to be expected of one of ordinary skill in the art (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a method for detecting cells infected with a recombinant poxvirus comprising at least two foreign

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genes by administering the DNA sequence to the cells, and to a method for identifying the recombinant poxvirus by administering the DNA sequence to the virus.

The state of the prior art and the predictability or lack thereof in the art. The art teaches that viruses and cells infected with viruses may be identified by laboratory methods which comprise contacting antibody probes directed against viral antigens with an infected cell or by contacting a sample containing the viral gene sequence with a complementary nucleic acid probe attached to a detectable label (See Mangana-Vougiouka et al. for a summary of the state of the art regarding identification of viruses and virus infected cells). The art does not teach that viruses or cells infected with viruses may be identified by administration of the gene sequence of the infecting virus. Therefore, the art teaches a high degree of unpredictability in identifying viruses or cells infected with viruses by administering viral genes.

The amount of direction or guidance present and the presence or absence of working examples important parameters in achieving successful therapy. Given the teachings of unpredictability which are found in the art, detailed teachings are required to be present in the specification to overcome the teachings of unpredictability found in the art. These teachings are absent. Although the applicant has provided working examples of inserting foreign genes into recombinant poxvirus, the examples provided do not describe a method for detecting infected cells or a method for identifying the recombinant poxvirus. No guidance is found anywhere in the specification directed to identification of a recombinant poxvirus by administering a viral gene.

The breadth of the claims and the quantity of experimentation needed: Because the art teaches that viruses and virus infected cells are identified by means not including administration of a viral gene and because there are no teachings in applicant's specification directed to any method for identifying a virus or virus infected cell by administering the viral gene, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention: The claimed invention is drawn to a cell comprising a recombinant poxvirus which reads on transgenic animals, including humans.

The state of the prior art and the predictability or lack thereof in the art: The art teaches a high degree of unpredictability in the ability to engineer transgenic animals.

The amount of direction or guidance present and the presence or absence of working examples important parameters in achieving successful therapy. Due to the unpredictability of engineering transgenic animals found in the art, detailed teachings are required to be present in the specification to overcome the teachings of unpredictability found in the art. These teachings are not found in the specification.

The breadth of the claims and the quantity of experimentation needed: Because the art of engineering transgenic animals is unpredictable, it would require undue

experimentation by one of skill in the art to be able to practice the claimed invention.

Inserting the word "isolated" would be remedial.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is not clear from the disclosure that the deposit of the recombinant poxvirus 00083008 meets all the criteria set forth in MPEP 608/01 (p)(C), items 1-3. Specifically, all of the required averments do not appear to be of record. Assurance of compliance may be in the form of a declaration. A suggested format for such a declaration is outlined below:

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following would be sufficient to overcome an objection and rejection based on a lack of availability of biological material.

1. Identifies declarant.
2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.
3. States that the deposited material has been accorded a specific (recited) accession number.
4. States that all restrictions on the availability to the public of the material will be irrevocably removed upon the granting of a patent.

5. States that the material has been deposited under conditions that ensure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 35 CFR 1.14 and 35 USC 122.

6. States that the deposited material will be stored with all care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case at least thirty (30) years after the date of a deposit or for the enforceable life of the patent, whichever is longer.

7. Acknowledges the duty to replace the deposit should the depository be unable to furnish a sample when requested due to the condition of the deposit.

8. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10 and 13-22, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Paoletti et al. (US Patent No: 5,744,141, April 1998).

The claimed invention is drawn to a recombinant poxvirus comprising at least two foreign genes, wherein the genes are inserted into different insertion sites of the viral genome, wherein the genes have at least 50% homology or 65-70% homology, wherein the genes are derived from a flavivirus, a dengue virus, wherein the genes are derived from at least two different serotypes of the virus, wherein the genes are at least two PrM genes, wherein the poxvirus is replication deficient or incompetent in mammalian cells, including human cells, wherein the poxvirus is a vaccinia virus, wherein the genes are inserted into a naturally occurring deletion site and/or into a intergenic region.

The claimed invention is also drawn to a medicament or vaccine with the recombinant poxvirus, a pharmaceutical composition comprising the recombinant poxvirus and a pharmaceutically acceptable carrier, diluent, adjuvant and/or additive, a recombinant poxvirus vaccine or composition inducing an immune response of a living animal, including a human, a method for inducing an immune response in a living animal, including a human, comprising administering a therapeutically effective amount of the recombinant poxvirus to the animal or human, a cell comprising the recombinant poxvirus, a method for producing a recombinant poxvirus comprising the steps: infecting a cell with a poxvirus; transfecting the infected cell with a vector construct, a gene heterologous to the poxviral genome, a genomic poxvirus sequence directing the integration of the heterologous gene into an insertion site; identifying and isolating the recombinant poxvirus; repeating the above steps using the recombinant poxvirus obtained from the steps above for infecting the cell and an additional vector comprising

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a gene heterologous to the poxvirus genome and homologous to the gene of the first vector.

Paoletti et al. teaches a recombinant poxvirus, such as vaccinia virus, containing foreign DNA from flavivirus, such as dengue. The recombinant poxvirus generates an extracellular particle containing flavivirus E and M proteins (Abstract). The foreign genes were inserted at different locations on the vaccinia virus genome (Example 5). The genetic recombination of genes can be between homologous and not perfectly homologous section of DNA (column 2, lines 26-33). Paoletti teaches recombinant poxvirus genes are derived from two different serotypes of the flavivirus, dengue type 2 and dengue type 4 (column 4, lines 31-39). The recombinant poxvirus, vaccinia virus, contains two PrM genes, dengue serotypes 2 PrM and dengue serotypes 4 PrM genes (column 4, lines 31-50). Paoletti teaches the genes are inserted in the open reading frame of the vaccinia virus which is a naturally occurring region of the genome (column 1, lines 55-57).

Paoletti teaches the replication deficient recombinant poxvirus, which expresses gene products of a flavivirus gene, for use as vaccines which provide protective immunity against flavivirus infections (column 1, lines 30-35). The vaccine for inducing an immunological response includes a carrier and a recombinant poxvirus containing, in a non-essential region, DNA from a flavivirus (column 5, lines 40-45).

Paoletti teaches a method for constructing the recombinant poxvirus for expression of foreign genes by inserting genes into a live poxvirus; inserting the DNA sequence into the virus particularly at an open reading frame from a non-pox source;

placing into a plasmid construct into which DNA homologous to a section of DNA of the poxvirus has been inserted; the DNA gene sequence to be inserted is ligated to a promoter; the promoter-gene linkage is flanked on both ends by DNA homologous to a DNA sequence flanking a region of pox DNA; the plasmid construct is amplified and isolated; the isolated plasmid containing the DNA gene sequence to be inserted is transfected into a cell culture along with the poxvirus. Recombination between homologous pox DNA in the plasmid and the viral genome gives a poxvirus modified by the presence of foreign DNA sequences. (column 1, lines 42-67 and column 2, lines 1-5)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paoletti et al. (US Patent No: 5,744,141, April 1998) as applied to claims 1-8, 10 and 13-25 above, in view of Men et al. (Vaccine, 2000, Vol. 18, p. 3113-3122).

The claimed invention described above wherein the vaccinia virus is a Modified Vaccinia Ankara (MVA) virus and the poxvirus is replication deficient or replication incompetent in mammalian cells. The teachings of Paoletti are described above. Paoletti et al. do not teach using the vaccinia virus strain, Modified Vaccinia Ankara (MVA) virus. Paoletti does not particularly point out that poxvirus is replication deficient or replication incompetent in mammalian cells.

Men et al. teaches the use of the highly attenuated, replication-deficient modified vaccinia Ankara (MVA) as a vector to construct recombinants for expression of the major envelope glycoprotein of one or more dengue virus serotypes. Men evaluated the protective immunity in animal models, e.g. mice and monkeys, and recognized the potential efficacy of recombinant MVA-DEN2 to protect primates against dengue infection suggest that the construction and evaluation of MVA recombinants expressing other serotypes of dengue virus for use as a tetravalent vaccine strategy might be warranted. (p. 3113, Abstract)

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the MVA strain of poxvirus for vaccine preparation.

The person of ordinary skill in the art would have been motivated to make that modification because MVA is a highly attenuated strain that is replication-deficient in mammals, and reasonably would have expected success because of the teachings of Men et al.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Paoletti et al. (US Patent No: 5,744,141, April 1998). The claimed invention described above wherein the genes are 4 PrM genes. The teachings of Paoletti are described above. Paoletti does not teach four serotypes of dengue and four PrM genes.

Paoletti teaches three serotypes of dengue, types 1, 2 and 4, with PrM genes. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use all four serotypes of dengue.

The person of ordinary skill in the art would have been motivated to make that modification because dengue has additional serotypes and reasonably would have expected success because of the PrM genes in all serotypes of dengue virus.

Claims 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paoletti et al. (US Patent No: 5,744,141, April 1998). The teachings of Laoletti are described above.

The claimed invention described above and further drawn to a kit comprising two or more vectors, each comprising a gene under transcriptional control of a poxviral expression control element, wherein the genes included in the different vectors are homologous genes, wherein each gene is flanked by a poxviral DNA sequence capable of directing the integration of the gene into a poxviral genome, and means for identifying and/or selecting recombinant poxviruses, which have homologous genes in their genome, wherein each gene of each vector is in a different insertion site of the poxviral genome.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to put the components of the method in a kit for convenience.

The person of ordinary skill in the art would have been motivated to make that modification because of the pharmaceutical applications of the recombinant poxvirus comprising foreign genes and reasonably would have expected success because of the teachings of Paoletti.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Hurt whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

May 26, 2006


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